6.0 510 (k) SUMMARY

SUBMITTED BY:

Mari A. Meyer
Regulatory Affairs Specialist
DiaSorin Inc.
1951 Northwestern Avenue
P.O. Box 285
Stillwater, MN 55082-0285
Phone (651) 351-5635
Fax (651) 351-5669
E-mail: mari.meyer@diasorin.com

NAME OF DEVICE:

Trade Name: DiaSorin LIAISON® TOXO IgM

Common Names/Descriptions: Immunoassay for the detection of IgM antibodies to *Toxoplasma gondii*

Classification Names: Enzyme Linked Immunosorbent Assay, Toxoplasma

Product Code: LGD

PREDICATE DEVICES: DiaSorin Toxoplasma IgM ELISA Kit (K963289)

DEVICE DESCRIPTION:

INTENDED USE:

The DiaSorin LIAISON® Toxo IgM assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the presumptive qualitative determination of IgM antibodies to *Toxoplasma gondii* in human serum. The LIAISON® Toxo IgM can be used as an aid in the presumptive diagnosis of acute or recent *Toxoplasma gondii* infection. It is recommended that the LIAISON® Toxo IgM assay be performed in conjunction with a *Toxoplasma gondii* IgG assay.

This assay has not been cleared/approved by the FDA for blood/plasma screening.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, neonatal specimens, or infants.

KIT DESCRIPTION:

The method for qualitative determination of IgM antibodies to *Toxoplasma gondii* (anti-Toxo IgM) is an antibody capture chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Analyzer. The principal components of the test are magnetic particles (solid phase) coated with IgG to human IgM (mouse, monoclonal), *Toxoplasma gondii* antigen, and a conjugate of mouse monoclonal antibodies to *Toxoplasma gondii* linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, IgM antibodies present in diluted calibrators, samples or controls bind to the solid phase. During the second incubation, the mouse monoclonal antibody conjugate reacts with *Toxoplasma gondii* antigen previously added and the immune complex thus formed reacts with IgM already bound to the solid phase. After each incubation, the unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal, and therefore the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of anti-Toxo IgM in calibrators, samples or controls.

PERFORMANCE DATA:

COMPARATIVE CLINICAL TRIALS:
A total of 892 prospectively collected samples were tested – 613 collected from the U.S and 279 collected from Europe. The U.S. collection included 200 samples from pregnant women. The testing was performed at three sites – a hospital, a physician's laboratory, and at DiaSorin. All samples were tested with the LIAISON® Toxo IgG Assay and an enzyme immunoassay, ELISA. Equivocal results were not repeat tested per the manufacturers' recommendations; these results were not included in the calculations of overall agreement.

U.S. Prospective samples:

LIAISON® Toxo IgM Results	DiaSorin Toxo IgM ELISA Results			
	Positive	Equivocal	Negative	Total
Positive (>= 10.0 AU)	1	0	0	1
Equivocal (8.0 - 9.9 AU)	1	0	1	2
Negative (< 8.0 AU)	1	1	408	410
Total	3	1	409	413

	Percent Agreement		Exact 95% confidence interval
Positive	33.3%	(1/3)	0.8 – 90.6%
Negative	99.8%	(408/409)	98.7 - 99.9%
Overall	99.3 %	(409/412)	97.9 – 99.9%

European Prospective sample:

LIAISON® Toxo IgM Results	DiaSorin Toxo IgM ELISA Results			
	Positive	Equivocal	Negative	Total
Positive (>= 10 AU)	41	0	3	44
Equivocal (8.0- 9.9 AU)	3	1	0	4
Negative (< 8.0 AU)	1	7	223	231
Total	45	8	226	279

	Percent Agreement		Exact 95% confidence interval
Positive	91.1%	(41/45)	78.0 – 97.5%
Negative	98.7%	(223/226)	96.2 - 99.7%
Overall	94.9%	(265/279)	91.7 – 97.3%

Prospective samples: *Pregnant Women*

LIAISON® Toxo IgM Results	ELISA Results			Total
	Positive	Equivocal	Negative	
Positive	1	0	1	2
Equivocal	1	0	0	1
Negative	1	2	194	197
Total	3	2	195	200

	Percent Agreement		Exact 95% confidence interval
Positive:	33.3%	(1/3)	0.8 – 90.6%
Negative:	99.5%	(194/195)	97.2 – 99.9%
Overall:	98.5%	(195/198)	95.6 – 99.7%

CDC PANEL STUDY:
The CDC (Centers for Disease Control and Prevention) Toxoplasma 1998 Human Serum Panel was tested by LIAISON® Toxo IgM assay. The panel is comprised of 100 frozen blinded specimens: 32 Toxoplasma IgM positive, 3 dilutions of three true Toxoplasma IgM positive, and 65 Toxoplasma IgM negative samples. Of the 6 IgM negative samples 30 were Toxoplasma IgG negative and 35 IgG positive. The data obtained were submitt to the CDC for analysis. The LIAISON® Toxo IgM Assay correctly detected the 32 out of the 32 IgM positives, 1 out of the three IgM positive dilutions, and 63 out of the 65 IgM negatives. Note: These results are presented as means to convey further information on the performance of this assay with a masked, characterized serum pan This does not imply endorsement of the assay by the CDC.

REPRODUCIBILITY:
An assay reproducibility study was conducted at two external US laboratories and at DiaSorin. A coded panel comprised of 9 frozen repository serum samples was prepared by DiaSorin and provided to each site for testing by the LIAISON® Toxo IgM assay. The panel contained 3 sets of serum samples. The sets were prepared to represent low to mid positive analyte levels. All panel members were divided into aliquots and stored frozen prior to testing. The same coded panel was tested at all three sites, in three replicates per run for ten runs. The results are summarized below.

ID#	N	mean (AU/mL)	within run S.D.	within run %CV	between run S.D.	between run %CV	between site S.D.	between site %CV	overall sd.	overall %CV
TMS1	90	33.1	3.08	9.18	9.12	12.54	6.04	18.26	7.57	22.89
TMS2	90	19.7	1.30	6.88	5.06	9.36	3.94	19.99	3.92	19.91
TMS3	90	*847*	*47.1*	*5.71*	*187*	*8.52*	*91.9*	*10.87*	*120.3*	*14.21*
TM1	90	24.4	1.70	6.65	7.38	10.33	6.23	25.48	6.10	24.96
TM2	90	34.0	2.08	5.74	12.26	9.77	11.49	33.78	10.71	31.48
TM3	90	26.7	1.95	7.17	7.55	8.20	6.03	25.57	6.04	22.63
TM4	90	25.9	1.65	6.14	8.35	8.67	7.17	27.65	6.91	26.67
TM5	90	14.0	0.97	6.83	3.57	8.73	2.44	17.46	2.64	18.84
TM6	90	18.8	0.88	4.52	6.00	8.62	5.16	27.41	4.95	26.31

*TMS3 dose was below the reading range of the assay. Precision calculations are based on signal (RLU) for this sample.

CROSS-REACTIONS:
Cross-reactivity studies for the LIAISON® Toxo IgM assay were designed to evaluate potential interference from IgM immunoglobulins directed against closely-related members of the herpes virus family (HSV-1, HSV-2, VZV, CMV),other organisms that may cause symptoms similar to Toxoplasmosis (i.e., EBV, rubella virus, hepatitis A virus, hepatitis B virus) and conditions that may result from atypical immune system activity (rheumatoid factor (RF), anti-nuclear antibodies (ANA)). Samples for these studies were selected using commercially available devices.

Organism/condition	**Number of Expected Negative Samples**	**LIAISON® Positive Result**
HAV Total	9	(0/9)
HBc Total	21	(0/21)
VZV IgM	8	(0/8)
Rubella IgM	7	(0/7)
CMV IgM	13	(0/13)
VCA IgM	14	(0/14)
HSV1-2 IgM	10	(0/10)
ANA	10	(0/10)
RF	10	(0/10)
HAMA	10	(0/10)
Total	**112**	**(0/112)**

No positive result was found for the samples when tested by LIAISON® Toxo IgM.

WARNING: Assay interference due to circulating antibodies against HIV and Hepatitis C virus has not been evaluated. The user is responsible for establishing cross-reactivity performance with these infectious agents.

INTERFERING SUBSTANCES:
Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides), icterus (at 20 mg/dL bilirubin).

6.0 510 (k) SUMMARY

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Stillwater, MN 55082-0285
Phone (651) 351-5635
Fax (651) 351-5669
E-mail: mari.meyer@diasorin.com

NAME OF DEVICE:

Trade Name: DiaSorin LIAISON® TOXO IgG

Common Names/Descriptions: Immunoassay for the detection of IgG antibodies to *Toxoplasma gondii*

Classification Names: Enzyme Linked Immunosorbent Assay, Toxoplasma

Product Code: LGD

PREDICATE DEVICES: Diamedix Is-Toxoplasma IgG ELISA Kit (K981498)

DEVICE DESCRIPTION:

INTENDED USE:
The LIAISON® Toxo IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer (Catolog number 15970) for the the qualitative determination of specific IgG antibodies to *Toxoplasma gondii* in human serum. The results of this assay can be used as an aid in the assessment of the patient's serological status to infection with *Toxoplasma gondii* and in the determination of immune status of individuals including pregnant women.

This assay has not been cleared/approved by the F.D.A for blood/plasma donor screening.

Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients, cord blood, neonatal specimens, or infants.

KIT DESCRIPTION: The method for qualitative determination of IgG antibodies to *Toxoplasma gondii* (anti-Toxo IgG) is an indirect chemiluminescence immunoassay (CLIA). All assay steps (with the exception of magnetic particle resuspension) and incubations are performed by the LIAISON® Analyzer. The principal components of the test are magnetic particles (solid phase) coated with *Toxoplasma gondii* and a conjugate of mouse monoclonal antibodies to human IgG linked to an isoluminol derivative (isoluminol-antibody conjugate). During the first incubation, *Toxoplasma gondii* antibodies present in diluted calibrators, samples or controls bind to the solid phase. During the second incubation, the monoclonal antibody conjugate reacts with anti-Toxo IgG that is already bound to the solid phase. After each incubation, unbound material is removed with a wash cycle. Subsequently, the starter reagents are added and a flash chemiluminescence reaction is thus induced. The light signal and therefore, the amount of isoluminol-antibody conjugate, is measured by a photomultiplier as relative light units (RLU) and is indicative of the presence of anti-Toxo IgG in calibrators, samples or controls.

PERFORMANCE DATA:

COMPARATIVE CLINICAL TRIALS:
A total of 887 prospectively collected samples were tested – 613 collected from the U.S and 274 collected from Europe. The U.S. collection included 200 samples from pregnant women. In addition, 200 archived samples from acute, chronic, and normal patients were tested. The testing was performed at four sites. All samples were tested with the LIAISON® Toxo IgG Assay and an enzyme immunoassay ELISA or Sabin Feldman Dye test.
Equivocal results were not repeat tested per the manufacturers' recommendations; these results were not included in the calculations of overall agreement.

U.S. Prospective samples:

LIAISON® Toxo IgG Results	ELISA Results			Total
	Positive	Equivocal	Negative	
Positive	78	1	8	87
Equivocal	3	4	7	13
Negative	4	4	304	313
Total	85	9	319	413

	Percent Agreement		Exact 95% confidence interval
Positive	91.8%	(78/85)	83.8 – 96.6%
Negative	95.3%	(304/319)	92.4 – 97.3%
Overall	93.5%	(386/413)	90.6 – 95.6%

European Prospective samples:

LIAISON® Toxo IgG Results	ELISA Results			Total
	Positive	Equivocal	Negative	
Positive	139	3	7	149
Equivocal	2	0	4	6
Negative	0	3	116	119
Total	141	6	127	274

	Percent Agreement		Exact 95% confidence interval
Positive	98.6%	(139/141)	94.9 – 99.8%
Negative	91.3%	(116/127)	85.0 – 95.6%
Overall	94.5%	(255/268)	91.9 – 97.4%

Prospective samples: *Pregnant Women*

LIAISON® Toxo IgG Results	ELISA Results			Total
	Positive	Equivocal	Negative	
Positive	48	2	3	53
Equivocal	1	0	1	2
Negative	1	1	143	145
Total	50	3	147	200

	Percent Agreement		Exact 95% confidence interval
Positive:	96.0%	(48/50)	86.3 – 99.5%
Negative:	97.3%	(143/147)	91.2 - 99.2%
Overall:	96.5%	(190/197)	92.8 – 98.6%

Retrospective Samples:

LIAISON® Toxo IgG Results	Sabin Feldman Dye test Results			Total
	Positive	Equivocal	Negative	
Positive	149	0	0	149
Equivocal	1	0	0	1
Negative	0	0	50	50
Total	150	0	50	200

	Percent Agreement		Exact 95% confidence interval
Positive	99.3%	(149/150)	96.3 - 99.9%
Negative	100.0%	(0/0)	92.0 – 100.0
Overall	99.5%	(49/50)	97.2 - 99.9%

CDC PANEL STUDY:

The CDC (Centers for Disease Control and Prevention) Toxoplasma 1998 Human Serum Panel was tested by LIAISON® Toxo IgG assay. The panel is comprised of 100 frozen blinded specimens, 70 Toxoplasma positive samples and 30 toxoplasma negative samples. The data obtained were submitted to the CDC for analysis. The LIAISON® Toxo IgG Assay correctly detected the 70 positive and the 30 negative specimens. Note: These results are presented as a means to convey further information on the performance of this assay with a masked, characterized serum panel. This does not imply endorsement of the assay by the CDC.

REPRODUCIBILITY:
An assay reproducibility study was conducted at two external US laboratories and at DiaSorin. A coded panel comprised of 9 frozen repository samples was prepared by DiaSorin and provided to each site for testing by the LIAISON® Toxo IgG assay. The panel contained samples prepared to represent low to mid positive analyte levels. All panel members were divided into aliquots and stored frozen prior to testing. The same coded panel was tested at all three sites, in three replicates per run for ten runs. The results are summarized below.

ID#	N	mean (IU/mL)	within run S.D.	within run %CV	between run S.D.	between run %CV	between site S.D.	between site %CV	overall sd.	overall %CV
TGS1	90	16.4	0.38	2.31	3.23	7.02	0.59	3.62	1.35	8.26
TGS2	89	33.4	0.18	2.88	1.46	5.07	0.81	2.42	0.46	5.94
TGS3	90	12.9	0.16	1.57	1.33	4.95	0.82	6.38	0.36	7.22
TG1	90	7.6	0.96	2.38	6.37	4.96	0.28	3.68	1.99	6.05
TG2	90	8.1	0.18	2.18	1.54	4.25	0.30	3.69	0.45	5.58
TG3	90	11.1	0.19	1.92	1.72	5.27	0.29	2.61	0.47	6.22
TG4	90	7.1	0.20	2.22	2.50	4.08	0.20	2.89	0.93	5.07
TG5	90	9.1	0.21	2.07	2.13	3.50	0.32	3.45	0.69	5.17
TG6	90	10.4	0.21	2.02	1.99	4.78	0.35	3.34	0.60	5.79

CROSS-REACTIONS:
Cross-reactivity studies for the LIAISON® Toxo IgG assay were designed to evaluate potential interference from IgG immunoglobulins directed against closely-related members of the herpes virus family (HSV-1, HSV-2, VZV, CMV), other organisms that may cause symptoms similar to Toxoplasmosis (i.e., EBV, rubella virus, hepatitis A virus, hepatitis B virus) and conditions that may result from atypical immune system activity [rheumatoid factor (RF), anti-nuclear antibodies (ANA)]. Samples for these studies were selected using commercially available devices.

Organism/condition	**Number of Expected Negative Samples**	**LIAISON® Positive Result**
HAV Total	12	(0/12)
HBc Total	17	(0/17)
VZV IgG	8	(0/8)
Rubella IgG	5	(0/5)
CMV IgG	10	(0/10)
VCA IgG	12	(0/12)
HSV1-2 IgG	2	(0/2)
ANA	7	(0/7)
RF	8	(0/8)
HAMA	7	(0/7)
Total	88	(0/88)

No positive result was found for the samples when tested by LIAISON® Toxoplasma IgG.

WARNING: Assay interference due to circulating antibodies against HIV and Hepatitis C virus has not been evaluated. The user is responsible for establishing cross-reactivity performance with these infectious agents.

INTERFERING SUBSTANCES:
Controlled studies of potentially interfering substances showed that the assay performance was not affected by hemolysis (at 1000 mg/dL hemoglobin), lipemia (at 3000 mg/dL triglycerides) or icterus (at 20 mg/dL bilirubin).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 8 2006

Ms. Mari Meyer
Regulatory Affairs Specialist
DiaSorin Inc.
1951 Northwestern Avenue
P.O. Box 285
Stillwater, MN 55082-0285

Re: k052499
Trade/Device Name: LIAISON® Toxo IgG
LIAISON® Toxo IgM
Regulation Number: 21 CFR 866.3780
Regulation Name: Toxoplasma gondii Serological Reagents
Regulatory Class: Class II
Product Code: LGD
Dated: January 5, 2006
Received: January 6, 2006

Dear Ms. Meyer:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (240)276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Sally A Hojvat

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K052499

Device Name: LIAISON® Toxo IgG

Indications For Use: The LIAISON® Toxo IgG assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the the qualitative determination of specific IgG antibodies to *Toxoplasma gondii* in human serum. The results of this assay can be used as an aid in the assessment of the patient's serological status to infection with *Toxoplasma gondii* and in the determination of immune status of individuals including pregnant women.

This assay has not been cleared/approved by the F.D.A for blood/plasma donor screening.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K052499

Indications for Use

510(k) Number (if known): K052499

Device Name: LIAISON® Toxo IgM

Indications For Use: The LIAISON® Toxo IgM assay uses chemiluminescent immunoassay (CLIA) technology on the LIAISON® Analyzer for the presumptive qualitative determination of IgM antibodies to *Toxoplasma gondii* in human serum. The LIAISON® Toxo IgM can be used as an aid in the presumptive diagnosis of acute or recent *Toxoplasma gondii* infection. It is recommended that the LIAISON® Toxo IgM assay be performed in conjunction with a *Toxoplasma gondii* IgG assay.

This assay has not been cleared/approved by the F.D.A for blood/plasma donor screening.

Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

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